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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/777,920

02/07/2001

Jacques Dumas

BAYER 15 P3

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7590

04/13/2009

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EXAMINER

DESAI, RITA J

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

04/13/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/777,920	Applicant(s) DUMAS ET AL.	
	Examiner Rita J. Desai	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-5, 9, 10, 12, 14-18, 25, 27, 34- 37, 39, 40, 42 and 45-47 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 34 and 35 is/are allowed.
- 6) ☒ Claim(s) 2-5, 9, 10, 12, 14-18, 25, 27, 36, 37, 39, 40, 42 and 45-47 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/3/09 has been entered.

Claims 2-5, 9, 10, 12, 14-18, 25, 27, 34-37, 39, 40, 42 and 45-47 are pending in the application.

The rejection of the claims under 35 USC 112 first para has been withdrawn as applicants have amended the claims. Except on claims 36.

The claim has been amended to include treating colorectal cancer. Treating cancer is not predictable. The specifications has no data provided that would show that it indeed treats cancer.

Those of skill in the art recognize that in-vitro assays and or cell-cultured based assays are generally useful to observe basic physiological and cellular phenomenon such as screening the effects of potential drugs. However, clinical correlations are generally lacking. The greatly increased complexity of the in vivo environment as compared to the very narrowly defined and controlled conditions of an in-vitro assays does not permit a single extrapolation of in vitro assays to human diagnostic efficacy with any reasonable degree of predictability. In vitro assays cannot easily assess cell-cell interactions that may be important in a particular pathological state. Furthermore it is well known that in the art that cultured cells over a period of time, lose phenotypic characteristics associated with their normal counterpart cell type. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts in vivo. These differences stem from the dissociation of cells from a three dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation in vivo. Without this control, cellular metabolism may be more constant in vitro but may not be truly representative of the tissue from which the cells were derived. This has often

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led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences In Vitro). Further , although drawn specifically to cancer cells, Dermer (Bio/Technology, 1994, 12:320) teaches that , “Petri dish cancer” is a poor representation of malignancy, with characteristics profoundly different from the human disease. Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary type that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not. Yet normal or malignant cells in vivo are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 yrs. Clearly it is well known in the art that cells i culture exhibit characteristics different from those in vivo and cannot duplicate the complex conditions of the in vivo environment involved in host –tumor and cell-cell interactions.

Applicants refer to a NPL document to show how the test can be done, however there is no test data given, or any showing that tests have been done.

CORRELATION: IN VITRO /IN VIVO

The issue of “correlation” is related to the issue of the presence or absence of working examples. “Correlation” as used herein refers to the relationship between in vitro or in vivo animal model assays and a disclosed or a claimed method of use. An in vitro or in vivo animal model example in the specification, in effect, constitutes a “working example” if that example “correlates” with a disclosed or claimed method invention. If there is no correlation, then the examples do not constitute “working examples.” In this regard, the issue of “correlation” is also dependent on the state of the prior art. In other words, if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate. Even with such evidence, the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition. In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (reversing the PTO decision based on finding that in vitro data did not support in vivo applications). Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an in vitro or in vivo animal model example. A rigorous or an invariable exact correlation is not required, as stated in Cross v. Iizuka, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985): [B]ased upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed in vitro utility and an in vivo activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. (Citations omitted.)

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The unpredictability in the art is high and so it cannot be seen how it is enabled to treat colorectal cancer.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-5, 9, 10, 12, 14-18, 25, 27, 37, 39, 40, 42 and 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5547966 Atwal et al .

Applicants claims are drawn to compounds of the formula A-D-B

Wherein B is a pyridyl or quinoline, D is NHCONH, and A is a L-M-L' where in L is a phenyl, M is an O and L' is a phenyl pyridyl or an isoindoline.

L' phenyl is substituted by CORx and Rx is NRaRb.

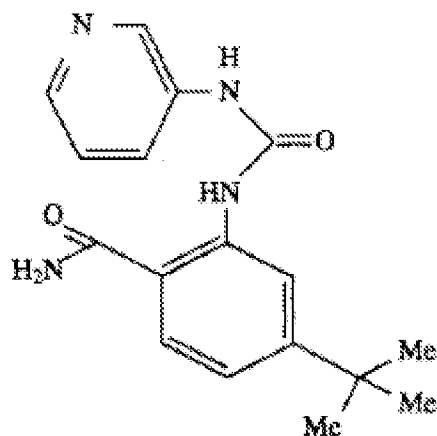
Scope & Content of Prior Art MPEP 2141.01

Atwal discloses the compound of the examples 15, 17

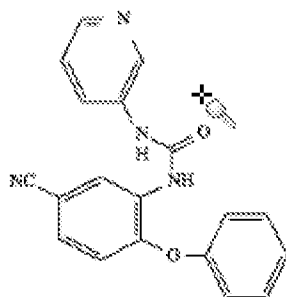
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**EXAMPLE 17**

**4-(1,1-Dimethylethyl)-2-[[[3-pyridinyl]
amino]carbonyl]-amino]benzamide**

**EXAMPLE 15**

N-(3-Cyano-2-phenoxyphenyl)-N'-(3-pyridinyl)urea



These compounds are also used as pharmaceuticals.

Difference between Prior Art and the claims MPEP 2141.02

The substituent CONH₂ is shown on the first aryl.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

Very close and similar compound as given in example 15 is shown. The difference being in the L' being substituted by COR_x.

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The prior art shows the substituent but on the first phenyl. Applicants substituent is on the second phenyl.

The compounds are very similar the prior art teaches the substituent CORx , Rx being NH2. One of skill in the art would have been motivated to put the same substituent on the L' and expect it to retain the pharmaceutical properties.

Conclusion

Claims 36, 2-5, 9, 10, 12, 14-18, 25, 27, 37, 39, 40, 42 and 45-47 stands rejected.

Claims 34, 35 are found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

April 07, 2009.